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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/525,797	03/15/2000	Athanasius A Anagnostou	5218-39B	9917

20792 7590 12/28/2004

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EXAMINER	
UNGAR, SUSAN NMN	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 12/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/525,797	ANAGNOSTOU ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *10 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *12-15,19-21 and 23-30* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *12-15,19-21 and 23-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 9/02/03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. The Amendment filed September 10, 2004 in response to the Office Action of March 10, 2004 is acknowledged and has been entered. Previously pending claims 12 and 21 have been amended, claims 27-30 have been added and claims 27-29 drawn to limitations other than the treatment of a solid vascularized tumor and claim 30 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions Claims 12-15, 19-21, 23-26 and claims 27-29, only as they are drawn to treatment of a solid vascularized tumor, are currently being examined.

2. Since applicant has received actions on the merits for the originally presented invention, that is a method of treating a solid vascularized tumor in a subject comprising administering a chemotherapeutic in conjunction with erythropoietin, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, the embodiments of claims 27-30 drawn to methods of treating conditions, other than solid vascularized tumors, associated with abnormal angiogenesis wherein treatment methods are drawn specifically to diabetic retinopathy, neovascular glaucoma, rheumatoid arthritis and psoriasis as specifically claimed in claim 30 have been withdrawn from consideration as being directed to a non-elected invention and a method of treating a solid vascularized tumor comprising administering a chemotherapeutic in conjunction with erythropoietin will be examined. See 37 C.F.R. § 1.142(b) and M.P.E.P. § 821.03. Newly submitted claims 27-30,as they read on limitations other than the treatment of a solid vascularized tumor comprising administering a chemotherapeutic in conjunction with erythropoietin, are independent or distinct from the invention originally claimed because the added claims are drawn to materially distinct methods which differ at least in objectives, method steps,

reagents and/or dosages and/or schedules used, response variables, and criteria for success from the originally presented invention.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. It is noted that newly added claim 28 would be subject to rejection under obviousness double patenting over claim 8 of US Patent No. 5/922,674, however, since a terminal disclaimer over US Patent No. 5/922,674 has already been filed in the case, in the interests of compact prosecution, the rejection will not be imposed here.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

5. Claims 12-15, 19-21, 23-26 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation of a subject "at risk of developing" recited in claims 12 and 21 has no clear support in the specification and the claims as originally filed. A review of the specification reveals support for the newly added limitations drawn to cerebellar hemangioblastoma, ductal carcinoma of the breast and squamous cell cancer of the larynx on page 5, lines 4-20, however there is no support for the limitation of subjects at risk of developing said cancers. The subject matter claimed in claims 12-15, 19-21, 23-26 broadens the scope of the invention as originally disclosed in the specification.

Claim Rejections - 35 USC 102

6. Claims 12-15, 19-21, 23-27, 29 are rejected under 35 USC 102(b) for the reasons previously set forth in the paper mailed March 10, 2004 and further for the reasons set forth below.

It is noted that Bukowski et al, of record, specifically states that the cisplatin study population consisted of 441 chemotherapy patients with various tumor types from community-based oncology practices nationwide, thus it is assumed for examination purposes that patients with the instantly claimed cancers are included in this group.

The claims are drawn to a method of treating a solid vascularized tumor in a subject in need of such treatment comprising administering cisplatin in conjunction with erythropoietin in an amount effective to enhance suppression of endothelial growth associated with administration of cisplatin wherein the subject is afflicted with a solid vascularized tumor selected from cerebellar hemangioblastoma, ductal carcinoma of the breast or squamous cell cancer of the larynx (claim 12), wherein said erythropoietin is administered concurrently with cisplatin (claim 13), prior to cisplatin (claim 14),after cisplatin (claim 15), wherein said cisplatin is administered intravenously (claim 19), wherein said erythropoietin is administered intravenously (claim 20), a method of treating a solid vasularized tumor comprising administering cisplatin in conjunction with erythropoietin wherein the erythropoietin is administered in an amount from about 750 U/Kg to about 2,000 U/kg and said subject is afflicted with a solid vascularized tumor selected from cerebellar hemangioblastoma, ductal carcinoma of the breast or squamous cell cancer of the larynx (claim 21), wherein said erythropoietin is administered concurrently with cisplatin (claim 23), wherein said cisplatin is administered intravenously (claim 24), wherein said erythropoietin is administered intravenously (claim 25), wherein said cisplatin is administered IV, IM, IP, SC, IT or IP (claim 26), a method of treating a condition/a solid vascularized tumor, associated with abnormal angiogenesis in a subject comprising administering erythropoietin in

conjunction with a chemotherapeutic agent, wherein said erythropoietin is administered in an amount effective to enhance suppression of endothelial growth (claim 27), wherein said chemotherapeutic agent is cisplatin (claim 29).

Bukowski et al teach as set forth previously, that is, Bukowski et al teach a successful phase IV study wherein erythropoietin was administered sc to 441 cancer patients in conjunction with cisplatin, wherein improvement in quality of life parameters was found wherein the patients experienced improved energy level, activity level and overall well-being, wherein transfusion requirements were reduced wherein the patients are treated with 150 U/kg sc three times a week for 8 weeks so that by the end of week 2 the patients had received 900 U/kg of erythropoietin and by the end of week 5 the patients had received about 2000 U/kg of erythropoietin. Since the specification does not teach a specific time for the administration of the erythropoietin and the claims are not limited to a specific time, the instant reference meets the dosage limitation of the claims. Further, since the reference teaches that the patients were receiving concomitant chemotherapy regimens, the erythropoietin was clearly being administered concurrently, prior to and after cisplatin administration. The method of the prior art comprises the same method steps as claimed in the instant invention, that is administering erythropoietin in conjunction with cisplatin to the same population, that is patients with solid vascularized tumors at the same dosage, thus the method is anticipated because the method will inherently lead to the enhanced suppression of endothelial growth associated with the administration of cisplatin. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993). Further, it is noted that the specification admits on the record that methods of administering chemotherapeutic drugs vary depending upon the specific agent used and would be known to one skilled in the art (p. 10, lines

24-29). One of skill would immediately envision the intravenous administration of both cisplatin and erythropoietin.

7. Claims 27-29 are rejected under 35 USC 102(b) as being anticipated by Bokkel et al (Proc. Am. Soc. Clin. Oncol., 1994,13, 30 Meet, 234).

The claims are drawn to a method of treating a condition/a solid vascularized tumor, associated with abnormal angiogenesis in a subject comprising administering erythropoietin in conjunction with a chemotherapeutic agent, wherein said erythropoietin is administered in an amount effective to enhance suppression of endothelial growth (claim 27), wherein said chemotherapeutic is cyclophosphamide (claim 28), wherein said chemotherapeutic is cisplatin (claim 29).

Bokkel et al et al teach a method of treating ovarian cancer patients comprising administering erythropoietin in conjunction with cisplatin and/or cyclophosphamide (see abstract) wherein patients were treated with erythropoietin which was administered at 300 U/kg sc three times a week over the course of chemotherapy treatment so that by the end of week 1 the patients had received 900 U/kg of erythropoietin. Since the specification does not teach a specific time for the administration of the erythropoietin and the specification specifically teaches that erythropoietin administered in a range of about 750 U/kg to about 2000 U/kg supports endothelial growth suppression caused by a chemotherapeutic agents (p. 12), the instant reference meets the dosage limitation of the claims. The method of the prior art comprises the same method steps as claimed in the instant invention, that is administering erythropoietin in conjunction with cyclophosphamide and or cisplatin to the same population, that is patients with solid vascularized tumors at the same dosage, thus the method is anticipated because the method will inherently

lead to the enhanced suppression of endothelial growth associated with the administration of cisplatin. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. To the extent that Bukowski et al, Supra, does not specifically teach that the patients with various types of cancer include cerebellar hemangioblastoma, ductal carcinoma of the breast or squamous cell cancer of the larynx, Claims 12-15, 19-21, 23-27, 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bukowski et al, *Supra*.

The claims are drawn to a method of treating a solid vascularized tumor in a subject in need of such treatment comprising administering cisplatin in conjunction with erythropoietin in an amount effective to enhance suppression of endothelial growth associated with administration of cisplatin wherein the subject is afflicted with a solid vascularized tumor selected from cerebellar hemangioblastoma, ductal carcinoma of the breast or squamous cell cancer of the larynx (claim 12), wherein said erythropoietin is administered concurrently with cisplatin (claim 13), prior to cisplatin (claim 14),after cisplatin (claim 15), wherein said cisplatin is administered intravenously (claim 19), wherein said erythropoietin is administered intravenously (claim 20), a method of treating a solid vasularized tumor

comprising administering cisplatin in conjunction with erythropoietin wherein the erythropoietin is administered in an amount from about 750 U/Kg to about 2,000 U/kg and said subject is afflicted with a solid vascularized tumor selected from cerebellar hemangioblastoma, ductal carcinoma of the breast or squamous cell cancer of the larynx (claim 21), wherein said erythropoietin is administered concurrently with cisplatin (claim 23), wherein said cisplatin is administered intravenously (claim 24), wherein said erythropoietin is administered intravenously (claim 25), wherein said cisplatin is administered IV, IM, IP, SC, IT or IP (claim 26), a method of treating a condition/a solid vascularized tumor, associated with abnormal angiogenesis in a subject comprising administering erythropoietin in conjunction with a chemotherapeutic agent, wherein said erythropoietin is administered in an amount effective to enhance suppression of endothelial growth (claim 27), wherein said chemotherapeutic agent is cisplatin (claim 29).

Bukowski teaches as set forth above but does not specifically state that cerebellar hemangioblastoma, ductal carcinoma of the breast or squamous cell cancer of the larynx patients were included in the treatment groups.

However, if not included in the treatment groups, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have included patients with cerebellar hemangioblastoma, ductal carcinoma of the breast or squamous cell cancer of the larynx in the combined therapy treatment of cancer patients receiving chemotherapy and erythropoietin because it is clear from the information in the reference that the combination treatment is a pan cancer treatment which was successful over a wide range of cancer types. Thus one would have a reasonable expectation of success in treating patients with cerebellar hemangioblastoma, ductal carcinoma of the breast or squamous cell cancer of the

larynx with the protocol and the enhancement of endothelial growth suppression associated with administration of cisplatin would be intrinsic. One would have been motivated to include the patients with cerebellar hemangioblastoma, ductal carcinoma of the breast or squamous cell cancer of the larynx because it was found that the treated cancer patients experienced significantly improved energy level, activity level, and overall well-being.

10. No claims allowed.

11. All other objections and rejections recited in the paper mailed March 10, 2004 are hereby withdrawn.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at 571-272-0787. The fax phone number for this Art Unit is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 872-9306.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
Primary Patent Examiner
December 23, 2004